

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2007 Budget Request

Witness appearing before the
House Subcommittee on Labor-HHS-Education Appropriations

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March 16, 2006

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Mr. Chairman and Members of the Committee, I am pleased to present the Fiscal Year 2007 President's budget request for the NIH AIDS research programs, a sum of \$2,888,492,000, which is a decrease of \$15,172,000 below the comparable FY 2006 appropriation. This amount includes the total trans-NIH funding for intramural and extramural research, research management support, research centers, and basic and clinical research on HIV/AIDS, as well as the wide spectrum of its associated malignancies, opportunistic infections, co-infections and clinical complications.

WORLDWIDE PANDEMIC

The AIDS pandemic will continue to wreak devastating consequences around the world for decades to come in virtually every sector of society. The pandemic affects the future of families, communities, agriculture, business, healthcare, child development, education, national security, military preparedness, political stability, and national economic growth in countries around the globe. AIDS is the deadliest epidemic of our generation. The United Nations General Assembly's Declaration of Commitment on HIV/AIDS states, "...the global HIV/AIDS epidemic, through its devastating scale and impact, constitutes a global emergency and one of the most formidable challenges to human life and dignity, as well as to the effective enjoyment of human rights, which undermines social and economic development throughout the world and affects all levels of society..." Laurie Garrett, in *Foreign Affairs*, states: "First, HIV/AIDS is the most complex disease humanity has ever faced and presents it with unprecedented challenges of research and analysis. Second, new threats to stability and security may emerge as the pandemic escalates. Third, a well-conceived campaign to curtail the virus, particularly through the development of an effective HIV vaccine, could short circuit the attendant security concerns."

THE EPIDEMIC IN THE UNITED STATES

The U.S. HIV/AIDS epidemic continues to expand. According to the Centers for Disease Control and Prevention (CDC), HIV infection rates are continuing to climb among women, racial and ethnic minorities, young homosexual men, individuals with

addictive disorders, and people over 50 years of age. Many HIV-infected people are living with the benefits resulting from NIH-supported therapeutics research. The development of combination regimens including protease inhibitors has extended the length and quality of life for many HIV-infected individuals in the United States. However, the use of antiretroviral therapy (ART) is now associated with a series of serious side effects and long-term complications that may have a negative impact on mortality rates. More deaths occurring from liver failure, kidney disease, and cardiovascular complications are being observed in this patient population. The appearance of multi-drug resistant strains of HIV presents an additional serious public health concern. According to CDC, about one quarter of the HIV-infected population in the United States also is infected with hepatitis C virus (HCV). HCV progresses more rapidly to liver damage in HIV-infected persons and may also impact the course and management of HIV infection; and HIV may change the natural history and treatment of HCV. These data forebode an epidemic of even greater magnitude in the coming years.

THE NIH AIDS RESEARCH PROGRAM

NIH is the world's leader in AIDS research. NIH supports a comprehensive program of basic, clinical, and behavioral research on HIV infection, its associated co-infections, opportunistic infections, malignancies, and other complications. This represents a unique and complex trans-NIH, multi-disciplinary, global research program with the ultimate goals to better understand the basic biology of HIV, develop effective therapies to treat and control HIV disease, and design interventions to prevent new infections from occurring. Perhaps no other disease so thoroughly transcends every area of clinical medicine and basic scientific investigation, crossing the boundaries of the NIH Institutes and Centers. This diverse research portfolio demands an unprecedented level of scientific coordination and management of research funds to identify the highest priority areas of scientific opportunity, enhance collaboration, minimize duplication, and ensure that precious research dollars are invested effectively and efficiently.

It is the unique role of the Office of AIDS Research (OAR), part of the NIH Office of the Director, to coordinate the scientific, budgetary, and policy elements of the NIH AIDS program; prepare an annual comprehensive trans-NIH strategic plan and budget for

all NIH-sponsored AIDS research; evaluate the AIDS research portfolio; identify and facilitate multi-institute participation in priority areas of research; and facilitate NIH involvement in international AIDS research activities. As such, the OAR represents the roadmap for NIH AIDS research, allowing NIH to pursue a united research front against the pandemic.

SETTING RESEARCH PRIORITIES: Trans-NIH Plan and Budget

The OAR develops the annual *NIH Plan for HIV-Related Research*, based on the most compelling scientific priorities that will lead to better therapies and prevention strategies for HIV infection and AIDS. OAR has established an effective model for developing a consensus on the scientific priorities of the Plan, utilizing advice from planning groups composed of NIH scientists and experts from academia, industry, and representatives from the AIDS community. The Plan serves as the framework for developing the annual NIH AIDS budget; for determining the use of NIH AIDS-designated dollars; for tracking and monitoring expenditures; and for informing the scientific community, the public, and the AIDS-affected community about NIH AIDS research priorities.

The over-arching themes of the AIDS research plan are: a strong foundation of basic science; research to prevent and reduce HIV transmission, including vaccines, microbicides, and behavioral interventions; research to develop better therapies for those who are already infected; international research, particularly to address the pandemic in developing countries; and biomedical and behavioral research targeting the disproportionate impact of AIDS on minority populations in the United States.

In consultation with the Director of NIH, the OAR Director determines the total annual AIDS research budget. The Institutes and Centers submit their AIDS budget requests to OAR, and the OAR establishes their AIDS research budgets, in accordance with the priorities of the Plan, at each step of the budget development process.

FUNDING HIGHEST PRIORITY RESEARCH: Trans-NIH Portfolio Review

Last year, OAR initiated a unique, innovative, multi-tiered comprehensive trans-NIH review of all grants and contracts supported with AIDS-designated funds scheduled

to recompete in FY 2006. OAR convened a group of eminent non-government experts to assist in this task, taking into account the evolving scientific opportunities to address the domestic and international AIDS epidemic. As a result of this review, OAR directed the transfer of funds to better manage the AIDS research portfolio. This highly successful process provided a new model to ensure that AIDS-designated research dollars support the highest priority science. This process has now been implemented as an integral component of the annual OAR strategic planning and budget process.

To develop the FY 2007 budget request, OAR again initiated a comprehensive trans-NIH review of all grants and contracts supported with AIDS-designated funds scheduled to recompete in FY 2007. OAR carefully reviewed the mix of investments in key priority areas of research in view of the current epidemic. This budget request reflects OAR's redirecting of AIDS funds to the highest priority projects and new scientific opportunities in FY 2007.

CRITICAL PRIORITIES FOR FY 2007: Prevention Research

In FY 2007, the highest priorities are in the area of prevention research. This budget request places highest priority on the discovery, development, and testing of additional HIV vaccine candidates, including funding to move promising vaccine candidates into large-scale clinical trials to evaluate the potential for efficacy. NIH has now conducted or initiated approximately 80 Phase I and two Phase II clinical trials of nearly 50 vaccine candidates, individually or in combination, in human volunteers in collaboration with academic investigators and industry co-sponsorship, and with the support of communities and government officials where the trials are being conducted. The evaluation of an HIV vaccine candidate will require extensive testing in the United States and in international settings where there is a high incidence of HIV.

Other prevention research priorities include the development of topical microbicides, strategies to prevent mother-to-child transmission, including a better understanding of risk associated with breast-feeding, management of sexually transmitted diseases (STDs), and behavioral research strategies, including interventions related to drug and alcohol use.

In addition, the experts who assisted in the portfolio analysis recommended that OAR redirect funds to support new innovative “second generation” prevention strategies, providing seed funds to newer areas of promising investigation to prevent HIV transmission, such as circumcision, early treatment of co-infections, use of antiretroviral therapy as prevention, cervical barrier methods, addiction treatment/substitution therapy, and combination prevention strategies. OAR will provide additional funds to the NIH Institutes and Centers for these new prevention strategies.

THERAPEUTICS RESEARCH

Important challenges remain in the area of therapeutics research. A growing proportion of patients receiving therapy are demonstrating treatment failure, experiencing serious drug toxicities and side effects, and developing drug resistance. The increasing incidence of metabolic disorders, cardiovascular complications, major organ dysfunction, and physical changes associated with current antiretroviral drugs underscores the critical need for new and better treatment regimens. Improved regimens also are needed to treat HIV co-infections such as hepatitis B and C, as well as other opportunistic infections to reduce drug interactions and problems with adherence to complicated treatment regimens. A high priority of NIH-sponsored AIDS therapeutics research continues to be the development of better drugs and therapeutic regimens that are less toxic and have fewer side effects, limit the development of drug resistance, enter viral reservoirs to inhibit viral replication, promote easier adherence, and are less expensive and more readily accessible.

INTERNATIONAL AIDS RESEARCH

NIH bears a unique responsibility to address the global epidemic, with priority on the urgent need for more affordable and sustainable prevention and treatment approaches that can be implemented in resource-limited nations. The high incidence of Hepatitis B and C, malaria, and tuberculosis (TB) in many of these nations further complicates the treatment and clinical management of HIV-infected individuals. NIH international AIDS research includes: development of HIV vaccine candidates and chemical and physical barrier methods, such as microbicides; behavioral strategies; strategies to prevent mother-

to-child transmission; therapeutics for HIV-related co-infections and other conditions; and approaches to using ART in resource-poor settings. NIH supports international training programs and initiatives that help build research infrastructure and laboratory capacity. Most of these funds are awarded to U.S.-based investigators to conduct research in collaboration with international collaborators; some funds are awarded directly to investigators in international research institutions.

WOMEN AND MINORITIES

NIH research has demonstrated that women progress to AIDS at lower viral load levels and higher CD4 counts than men. Women also experience different clinical manifestations and complications of HIV disease. These findings may have implications for care and treatment of HIV-infected women, particularly with antiretroviral therapy. NIH is exploring research questions about specific characteristics of women and girls that might play a role in transmission, acquisition, or resistance to HIV infection during different stages of the life course. We are focusing on the need for comprehensive strategies to decrease HIV transmission in affected vulnerable populations, and improve treatment options and treatment outcomes, including interventions that address the co-occurrence of other STDs, hepatitis, drug abuse, and mental illness; and interventions that consider the role of culture, family, and other social factors in the transmission and prevention of these disorders in minority communities. NIH continues to make significant investments to improve research infrastructure and training opportunities for minorities and will continue to ensure the participation of minorities in AIDS clinical trials, as well as in natural history, epidemiologic, and prevention studies.

SUMMARY

NIH-sponsored HIV/AIDS research continues to provide the important scientific foundation necessary to design, develop, and evaluate new and better vaccine candidates, therapeutic agents and regimens, and prevention interventions. The NIH's leadership role in the response to the AIDS pandemic is fundamental and unprecedented, and we have established a research program that is complex, comprehensive, multi-disciplinary, inter-disciplinary, and global. Further, this research investment is reaping even greater

dividends, as AIDS-related research is also unraveling the mysteries surrounding many other infectious, malignant, neurologic, autoimmune, and metabolic diseases. AIDS research has provided an entirely new paradigm for drug design, development, and clinical trials to treat viral infections. For example, the drug known as 3TC, developed to treat HIV/AIDS, is now the most effective therapy for chronic hepatitis B infection. Drugs developed to prevent and treat AIDS-associated opportunistic infections also provide benefit to patients undergoing cancer chemotherapy or receiving anti-transplant rejection therapy. AIDS research also is providing a new understanding of the relationship between viruses and cancer.

NIH is enhancing collaboration, minimizing duplication, and ensuring that research dollars are invested in the highest priority areas of scientific opportunity that will lead to new tools in the fight against AIDS. The legislative authorities of the OAR allow NIH to pursue a united research front against the global AIDS epidemic. We are deeply grateful for the continued support the Administration and this Committee have provided to our efforts.